chromosome 17

Humans normally have 46 chromosomes in each cell, divided into 23 pairs. Two copies of chromosome 17, one copy inherited from each parent, form one of the pairs. Chromosome 17 spans about 81 million DNA building blocks (base pairs) and represents between 2.5 and 3 percent of the total DNA in cells.

Identifying genes on each chromosome is an active area of genetic research. Because researchers use different approaches to predict the number of genes on each chromosome, the estimated number of genes varies. Chromosome 17 likely contains 1,200 to 1,300 genes that provide instructions for making proteins. These proteins perform a variety of different roles in the body.

Health Conditions Related to Chromosomal Changes

The following chromosomal conditions are associated with changes in the structure or number of copies of chromosome 17.

acute promyelocytic leukemia

A type of blood cancer known as acute promyelocytic leukemia is caused by a rearrangement (translocation) of genetic material between chromosomes 15 and 17. This translocation, written as t(15;17), fuses part of the *PML* gene from chromosome 15 with part of the *RARA* gene from chromosome 17. This mutation is acquired during a person's lifetime and is present only in certain cells. This type of genetic change, called a somatic mutation, is not inherited. The t(15;17) translocation is called a balanced reciprocal translocation because the pieces of chromosome are exchanged with each other (reciprocal) and no genetic material is gained or lost (balanced). The protein produced from this fused gene is known as PML-RARα.

The PML-RARα protein functions differently than the protein products from the normal *PML* and *RARA* genes. The *RARA* gene on chromosome 17 provides instructions for making a transcription factor called the retinoic acid receptor alpha (RARα). A transcription factor is a protein that attaches (binds) to specific regions of DNA and helps control the activity (transcription) of particular genes. Normally, the RARα protein controls the activity of genes important for the maturation (differentiation) of immature white blood cells beyond a particular stage called the promyelocyte. The *PML* gene on chromosome 15 provides instructions for a protein that acts as a tumor suppressor, which means it prevents cells from growing and dividing too rapidly or in an uncontrolled way. The PML protein blocks cell growth and division (proliferation) and induces self-destruction (apoptosis) in combination with

other proteins. The PML-RARα protein interferes with the normal function of both the PML and the RARα proteins. As a result, blood cells are stuck at the promyelocyte stage, and they proliferate abnormally. Excess promyelocytes accumulate in the bone marrow and normal white blood cells cannot form, leading to acute promyelocytic leukemia.

dermatofibrosarcoma protuberans

Translocation of genetic material between chromosomes 17 and 22, written as t(17;22), causes a rare type of skin cancer known as dermatofibrosarcoma protuberans. This translocation fuses part of the *COL1A1* gene from chromosome 17 with part of the *PDGFB* gene from chromosome 22. The translocation is found on one or more extra chromosomes that can be either linear or circular. When circular, the extra chromosomes are known as supernumerary ring chromosomes. This mutation is acquired during a person's lifetime and is present only in certain cells. This type of genetic change, called a somatic mutation, is not inherited.

The fused *COL1A1-PDGFB* gene provides instructions for making a combined (fusion) protein that researchers believe ultimately functions like the active PDGFB protein. In the translocation, the *PDGFB* gene loses the part of its DNA that limits its activity, and production of the COL1A1-PDGFB fusion protein is controlled by *COL1A1* gene sequences. As a result, the gene fusion leads to the production of a larger amount of active PDGFB protein than normal. Active PDGFB protein signals for cell growth and division (proliferation) and maturation (differentiation). Excess PDGFB protein abnormally stimulates cells to proliferate and differentiate, leading to the tumor formation seen in dermatofibrosarcoma protuberans.

Koolen-de Vries syndrome

Deletion of a small amount of genetic material (a microdeletion) on chromosome 17 can cause Koolen-de Vries syndrome. This disorder is characterized by developmental delay, intellectual disability, a cheerful and sociable disposition, and a variety of physical abnormalities.

Most people with Koolen-de Vries syndrome are missing a sequence of about 500,000 base pairs, also written as 500 kilobases (kb), at position q21.31 on chromosome 17. The exact size of the deletion varies among affected individuals, but it contains at least six genes including *KANSL1*. This deletion affects one of the two copies of chromosome 17 in each cell.

Because mutations in the *KANSL1* gene cause the same signs and symptoms as the deletion, researchers have concluded that the loss of this gene accounts for the features of Koolen-de Vries syndrome. The protein produced from the *KANSL1* gene is involved in controlling the activity of other genes and plays an important role in the development and function of many parts of the body. Although the loss of this gene

impairs normal development and function, its relationship to the specific features of Koolen-de Vries syndrome is unclear.

While Koolen-de Vries syndrome is usually not inherited, most individuals with the condition caused by a deletion have had at least one parent with a common variant of the 17q21.31 region of chromosome 17 called the H2 lineage. This variant is found in 20 percent of people of European and Middle Eastern descent, although it is rare in other populations. In the H2 lineage, a 900 kb segment of DNA, which includes the region deleted in most cases of Koolen-de Vries syndrome, has undergone an inversion. An inversion involves two breaks in a chromosome; the resulting piece of DNA is reversed and reinserted into the chromosome.

People with the H2 lineage have no health problems related to the inversion. However, genetic material can be lost or duplicated when the inversion is passed to the next generation. Researchers believe that a parental inversion is probably necessary for a child to have the 17q21.31 microdeletion most often associated with Koolen-de Vries syndrome, but other, unknown factors are also thought to play a role. So while the inversion is very common, only an extremely small percentage of parents with the inversion have a child affected by Koolen-de Vries syndrome.

Miller-Dieker syndrome

Miller-Dieker syndrome is caused by a deletion of genetic material near the end of the short (p) arm of chromosome 17. The signs and symptoms of Miller-Dieker syndrome are related to the loss of multiple genes in this region. The size of the deletion varies among affected individuals. The loss of a particular gene on chromosome 17, called *PAFAH1B1*, is responsible for the syndrome's characteristic sign of lissencephaly, a problem with brain development in which the surface of the brain is abnormally smooth. The loss of another gene, called *YWHAE*, in the same region of chromosome 17 increases the severity of lissencephaly in people with Miller-Dieker syndrome. Additional genes in the deleted region contribute to the varied features of Miller-Dieker syndrome.

Smith-Magenis syndrome

Most people with Smith-Magenis syndrome have a deletion of genetic material from a specific part of chromosome 17 called the Smith-Magenis syndrome critical region. This region is located on the short (p) arm of chromosome 17 at position 11.2 (written as 17p11.2). Although this region contains multiple genes, researchers believe that the loss of one particular gene, *RAI1*, in each cell is responsible for most of the physical, mental, and behavioral features of Smith-Magenis syndrome. The loss of other genes in the deleted region may help explain why the signs and symptoms of this condition vary among affected individuals.

other cancers

Changes in chromosome 17 have been identified in several additional types of human cancer. These genetic changes are somatic, which means they are acquired during a person's lifetime and are present only in certain cells. A particular chromosomal abnormality called an isochromosome 17q occurs frequently in some cancers. This abnormal version of chromosome 17 has two long (q) arms instead of one long arm and one short (p) arm. As a result, the chromosome has an extra copy of some genes and is missing copies of other genes.

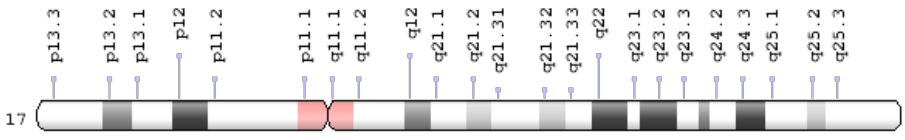
An isochromosome 17q is commonly found in a cancer of blood-forming tissue called chronic myeloid leukemia (CML). It also has been identified in certain solid tumors, including a type of brain tumor called a medulloblastoma and tumors of the brain and spinal cord known as primitive neuroectodermal tumors. Although an isochromosome 17q probably plays a role in both the development and progression of these cancers, the specific genetic changes related to cancer growth are unknown.

other chromosomal conditions

Other changes in the number or structure of chromosome 17 can have a variety of effects, including intellectual disability, delayed development, characteristic facial features, weak muscle tone (hypotonia), and short stature. These changes include an extra piece of chromosome 17 in each cell (partial trisomy 17), a missing segment of the chromosome in each cell (partial monosomy 17), and a circular structure called a ring chromosome 17. Ring chromosomes occur when a chromosome breaks in two places and the ends of the chromosome arms fuse together to form a circular structure.

Chromosome Diagram

Geneticists use diagrams called idiograms as a standard representation for chromosomes. Idiograms show a chromosome's relative size and its banding pattern, which is the characteristic pattern of dark and light bands that appears when a chromosome is stained with a chemical solution and then viewed under a microscope. These bands are used to describe the location of genes on each chromosome.



Credit: Genome Decoration Page/NCBI

Additional Information & Resources

MedlinePlus

- Encyclopedia: Chromosome
  https://medlineplus.gov/ency/article/002327.htm

Additional NIH Resources

- National Human Genome Research Institute: Chromosome Abnormalities
  https://www.genome.gov/11508982/

GeneReviews

- 17q12 Recurrent Deletion Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK401562
- 17q12 Recurrent Duplication
  https://www.ncbi.nlm.nih.gov/books/NBK344340
- KANSL1-Related Intellectual Disability Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK24676
- LIS1-Associated Lissencephaly/Subcortical Band Heterotopia
  https://www.ncbi.nlm.nih.gov/books/NBK5189
- Smith-Magenis Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1310

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  https://www.ncbi.nlm.nih.gov/pubmed?term=%28Chromosomes,+Human,+Pair+17%5BMAJR%5D%29+AND+%28Chromosome+17%5BTI%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22%5Bdp%5D

OMIM

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  http://omim.org/entry/608232
- MEDULLOBLASTOMA
  http://omim.org/entry/155255

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